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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/445,865	02/11/2000	PHILIP JOHN BURKE	ERD100	1461
7590	10/07/2003		EXAMINER	
Patrea L. Pabst Holland & Knight LLP One Atlantic Center 1201 West Peachtree Street Suite 2000 Atlanta, GA 30309-3400			NICKOL, GARY B	
			ART UNIT	PAPER NUMBER
			1642	
			DATE MAILED: 10/07/2003	

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/445,865	BURKE ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 20 August 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b])

a) The period for reply expires 3 months from the mailing date of the final rejection.
 b) The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
 ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. The proposed amendment(s) will not be entered because:

(a) they raise new issues that would require further consideration and/or search (see NOTE below);
 (b) they raise the issue of new matter (see Note below);
 (c) they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 (d) they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Attached.

3. Applicant's reply has overcome the following rejection(s): _____.
 4. Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
 5. The a) affidavit, b) exhibit, or c) request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Attached.
 6. The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
 7. For purposes of Appeal, the proposed amendment(s) a) will not be entered or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.
 Claim(s) objected to: 41.
 Claim(s) rejected: 29,31-33,40 and 42-44.
 Claim(s) withdrawn from consideration: _____.
 8. The proposed drawing correction filed on _____ is a)a) approved or b) disapproved by the Examiner.
 9. Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.
 10. Other: Attachment



Response to Arguments

Claims 29, 31-33, 40, and 42-43 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons of record in Paper No. 25, page 3.

Applicant's argue (Paper No. 26, page 4) that the use of the term "substituted" in a formula is well understood by those of ordinary skill in the art. In this case, applicants argue, any chemist would know exactly what was meant by the claim formula. Applicants further provide evidence in the form of excerpts from Tabor's medical encyclopedia and a textbook on organic chemistry. These arguments have been carefully considered but are not found persuasive. While the general term "substituted" may be understood by those of skill in the art, in this particular context, the claims remain indefinite because the identity of moieties, which are intended to be substituted, have not been distinctly described either structurally or by chemical name. Thus, applicant's arguments have not been found persuasive and the rejection is maintained.

Claims 29, 31-33, 40, and 42-44 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Friedlos *et al.* (Biochem. Pharmacol. 44(9) pages 1739-43, 1992, IDS.. **Friedlos#1**) and Friedlos *et al.* (Biochem. Pharmacol. 44(1), pages 25-31, 1992, IDS. **Friedlos#2**) in view of Jaiswal, A. (J.Biol.Chem. 269(20), pages 14502-08, 1994, IDS) for the reasons of record in Paper No. 25, pages 3-6.

Applicants argue (Paper No. 26, page 6) that there is no disclosure, suggestion, or even hint in the cited art that one should substitute NQO2 (and substrate thereof) for NQO2. (It is assumed

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for examination purposes that applicants intended to argue that there was no basis for substituting NQO1 for NQO2.) This argument has been considered but is not found relevant because the previous rejection was not based on substituting either enzyme. The claims only require that a target cell express NQO2, and the previous rejection held that although Friedlos#1 did not specifically characterize the target cells as expressing NQO2, any administration of the claimed compounds would anticipate target cells to be destroyed as expressing NQO2 since it was well known in the art at the time the invention was made that NQO2 was expressed in several human tissues including heart, lung, liver, skeletal muscle, kidney, and pancreas (See teachings of Jaisawl, Paper No. 23, page 5). Applicants have also argued that there is no suggestion in any of the cited art that one could obtain much more effective formation of cytotoxic species in the presence of NRH. This argument has been considered but is not found persuasive for the reasons of record. On the contrary, the prior art clearly suggests that the addition of NRH would enhance the formation of cytotoxic species because Friedlos#1 have shown that the relative inactivity of human DT diaphorase (NQO1) towards CB1954 *can be overcome* by the addition of NADH or NRH in human tumor cells. Further, since NQO1 and NQO2 catalyze related substrates with near equal efficiency (see Paper No. 23, page 5, 2nd paragraph) one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success that the addition of NRH would also enhance the formation of cytotoxic species in target cells that expressed NQO2. Thus, applicant's arguments have not been found persuasive and the rejection is maintained.

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Claim 41 remains objected to as being dependent upon a rejected base claim. Applicants proposed amendment was considered but failed to meet the criteria for allowable subject matter because the proposed amendment did not include all of the limitations of the base claim and any intervening claims. Further, the newly proposed amendment would require further searches and consideration as it is broader in scope than the originally filed claimed subject matter.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
October 3, 2003

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